

Ophthalmology Times  
**Research Scholar**  
Honoree Program

Significance of Early Outer Retinal Findings on  
En Face and Cross-Sectional Optical Coherence  
Tomography Imaging of Eyes with Macula-Off  
Rhegmatogenous Retinal Detachment

Tina Felfeli, MD

University of Toronto

November 5, 2020

# FINANCIAL DISCLOSURES:

No financial disclosures.

# MY ROLE IN THIS RESEARCH:

Please answer which of the following portions of the research you participated in:

- Conception and design of the work/project
- Acquisition of data
- Analysis and interpretation of data
- Creation and/or critical review of the presentation

# Background

- Macula-off rhegmatogenous retinal detachment (RRD) repair has variability in long-term visual recovery.
- Some factors may predict visual outcomes:
  - macular involvement
  - duration of macular detachment
  - preoperative visual acuity
  - timing of the surgical repair
- Additional factors that may predict visual outcomes:
  - height of macular detachment
  - pre-operative outer retinal corrugations
  - post-operative outer retinal folds
- These may be manifestations of chronicity and indicate more severe photoreceptor damage at the time of detachment.

# Objective

To determine the association of **early outer retinal pathology after macula-off RRD** on **structural en face and cross-sectional SD-OCT** images with **long-term** postoperative retinal microstructural changes and functional **outcomes**.

# Methods

## Study Design:

- Post-hoc analysis of a randomized controlled trial. ('PIVOT'; ClinicalTrials.gov identifier: NCT01639209)

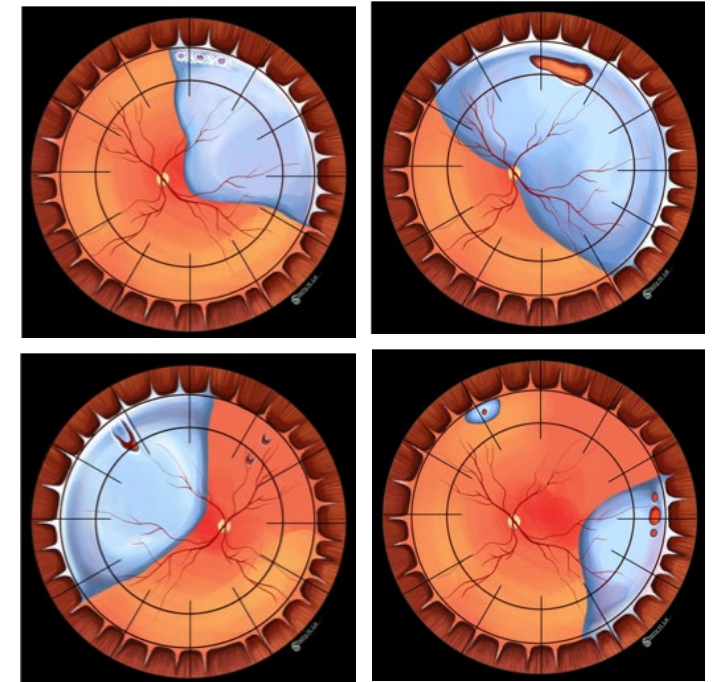
## Inclusion criteria:

- A single retinal break or group of breaks, within one clock hour (30°), in detached retina.
- All breaks in detached retina to lie above the 8 and 4 o'clock meridian.
- Breaks or lattice degeneration in attached retina at any location (even inferior) were allowed.



## The Pneumatic Retinopexy versus Vitrectomy for the Management of Primary Rhegmatogenous Retinal Detachment Outcomes Randomized Trial (PIVOT)

Roxane J. Hillier, MBChB, FRCOphth,<sup>1,2,3,4,\*</sup> Tina Felfeli, BSc,<sup>2</sup> Alan R. Berger, MD, FRCSC,<sup>1,2</sup> David T. Wong, MD, FRCSC,<sup>1,2</sup> Filiberto Altomare, MD, FRCSC,<sup>1,2</sup> David Dai, MSc,<sup>5</sup> Louis R. Giavedoni, MD, FRCSC,<sup>1,2</sup> Peter J. Kertes, MD, FRCSC,<sup>2,6,7</sup> Radha P. Kohly, PhD, FRCSC,<sup>2,6,7</sup> Rajeev H. Muni, MD, FRCSC<sup>1,2,6,\*</sup>



# Methods

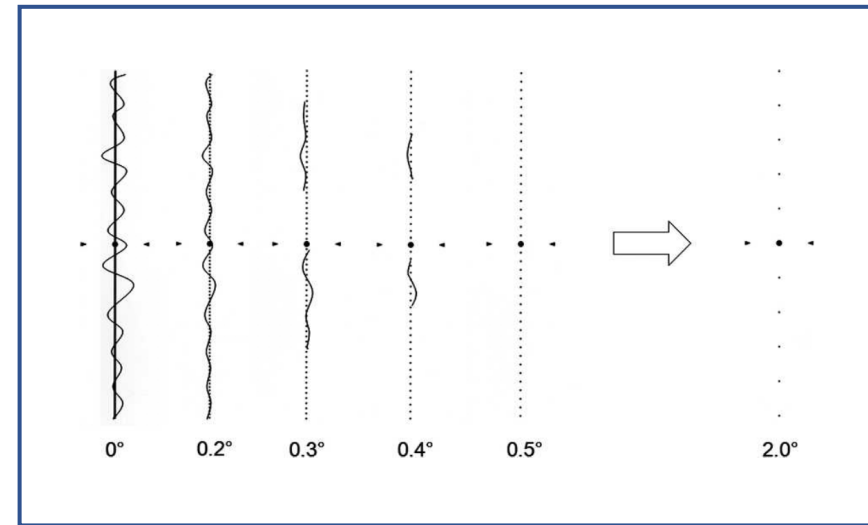
Functional outcomes

## Visual acuity

- Snellen chart at baseline and 1 month
- Early Treatment Diabetic Retinopathy Study (ETDRS) letters at 3, 6 and 12-month follow-ups using.

## Metamorphopsia

- M-Charts scores at 12-month follow-up.



# Methods Image Analysis

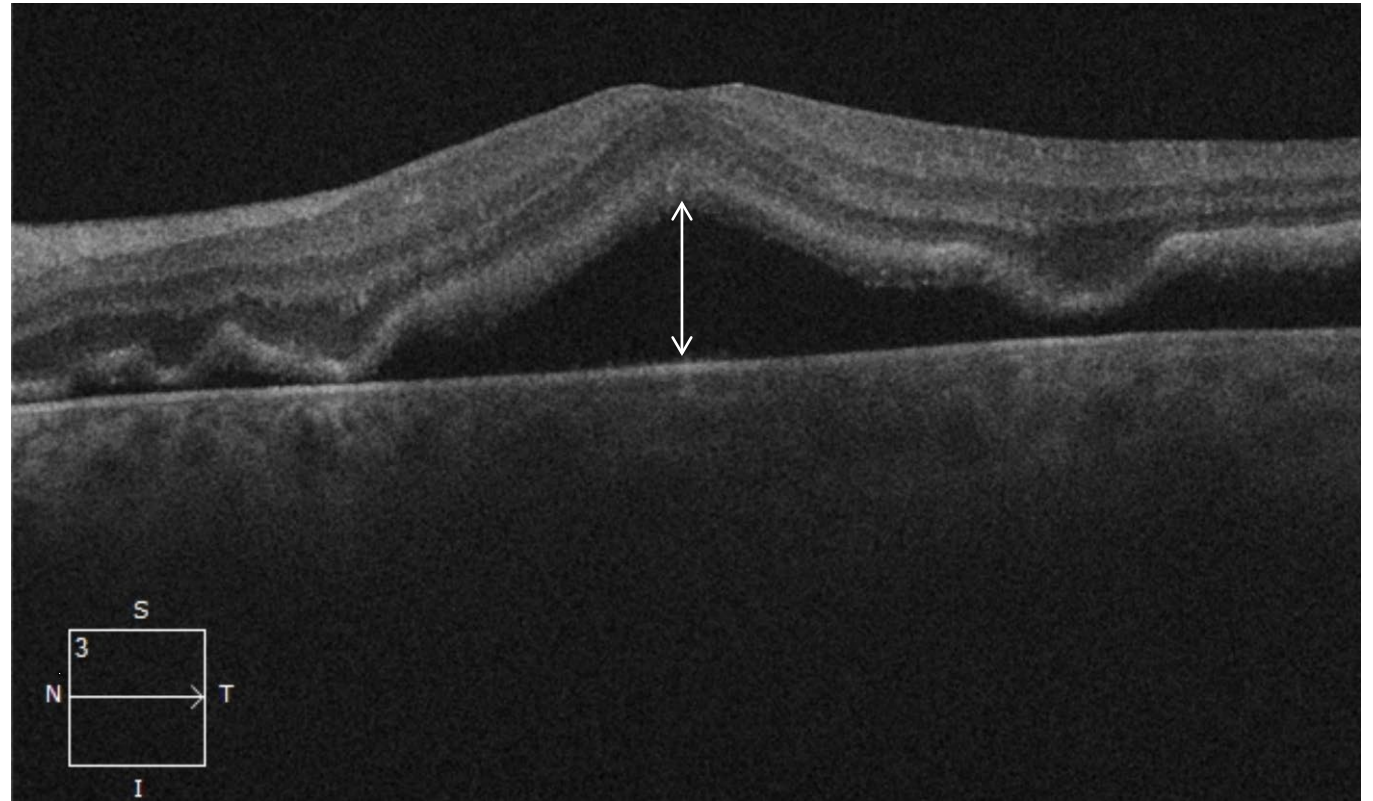
- SD-OCT, Cirrus™ HD-OCT, Carl Zeiss Meditec
  - five-line raster and macular-cube scans (6mm) in the horizontal meridian (all 5 scans were reviewed)
  - scans with signal strength of more than 6/10 were considered to be appropriate
- Baseline images graded by two independent graders and disagreements adjudicated by a third grader.
- Integrity of the outer retinal layers at 6 and 12 months graded by an external retinal image reading center.
  - external limiting membrane (ELM)
  - ellipsoid zone (EZ)
  - interdigitation zone (IZ)



# Methods Image Analysis

## Subretinal fluid height

- The distance between the outer surface of the detached neurosensory retina at the central fovea perpendicular to the RPE.<sup>1</sup>



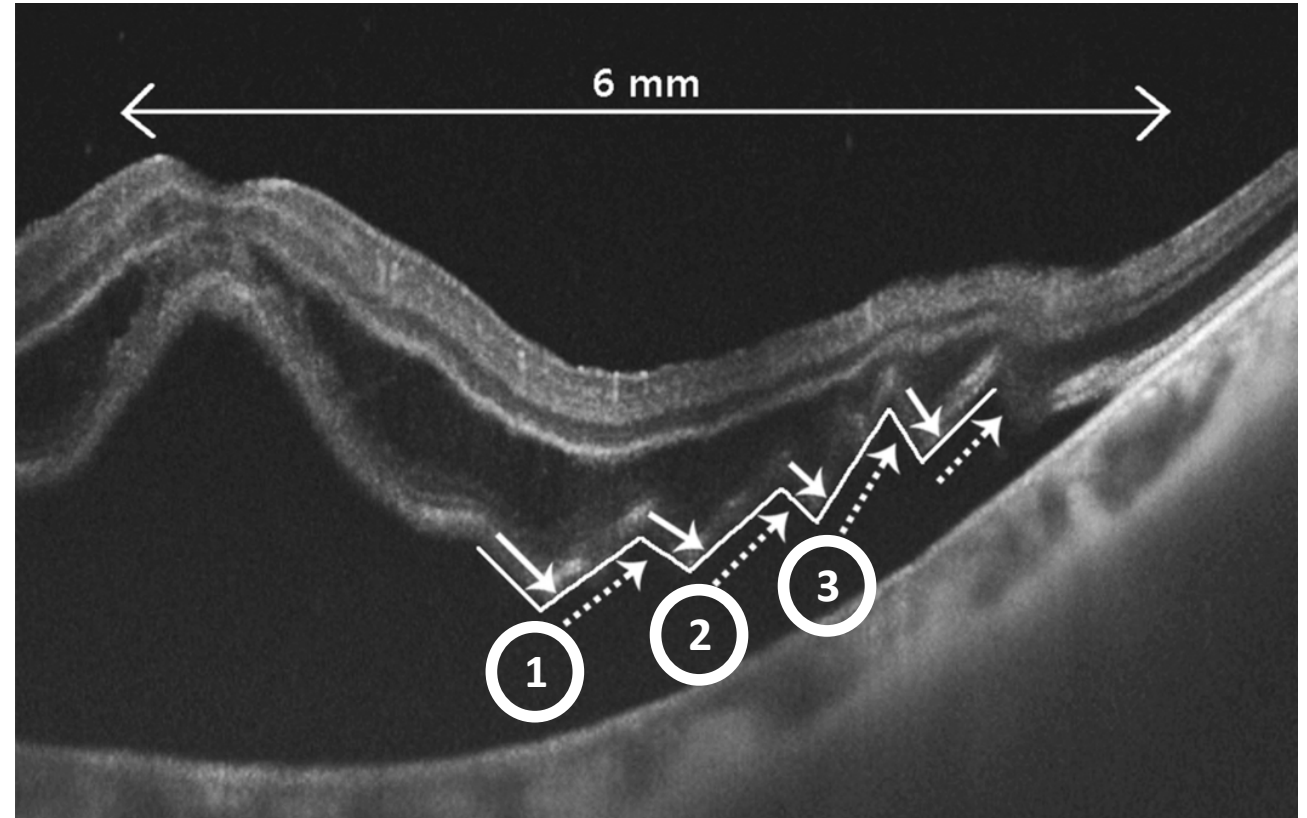
1. Leclaire-Collet A, Muraine M, Ménard JF, Brasseur G. Evaluation of Macular Changes Before and After Successful Retinal Detachment Surgery Using Stratus-Optical Coherence Tomography. Am J Ophthalmol 2006;142:176–179.



# Methods Image Analysis

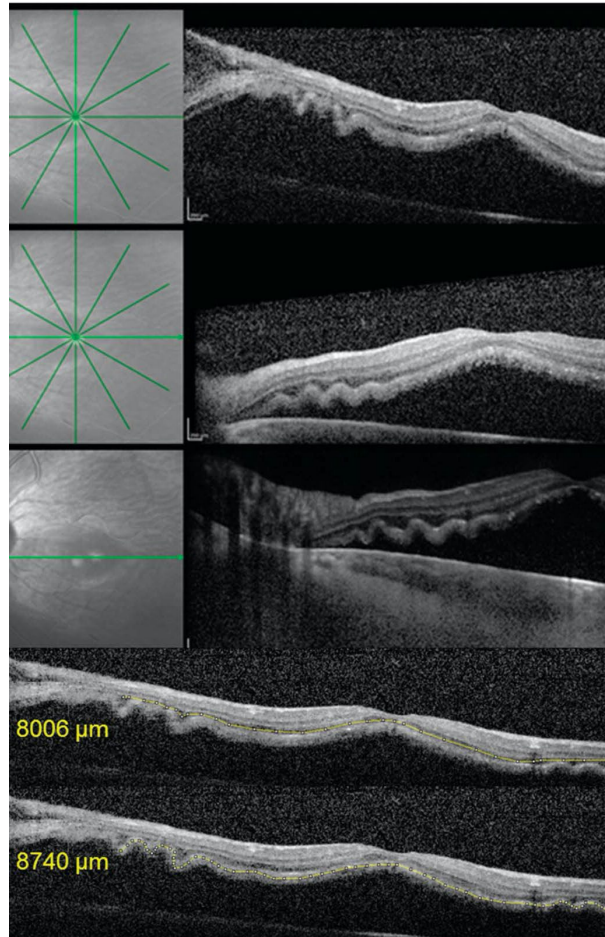
## Outer retinal corrugations

- > 3 combinations of up and down reflections.<sup>1</sup>



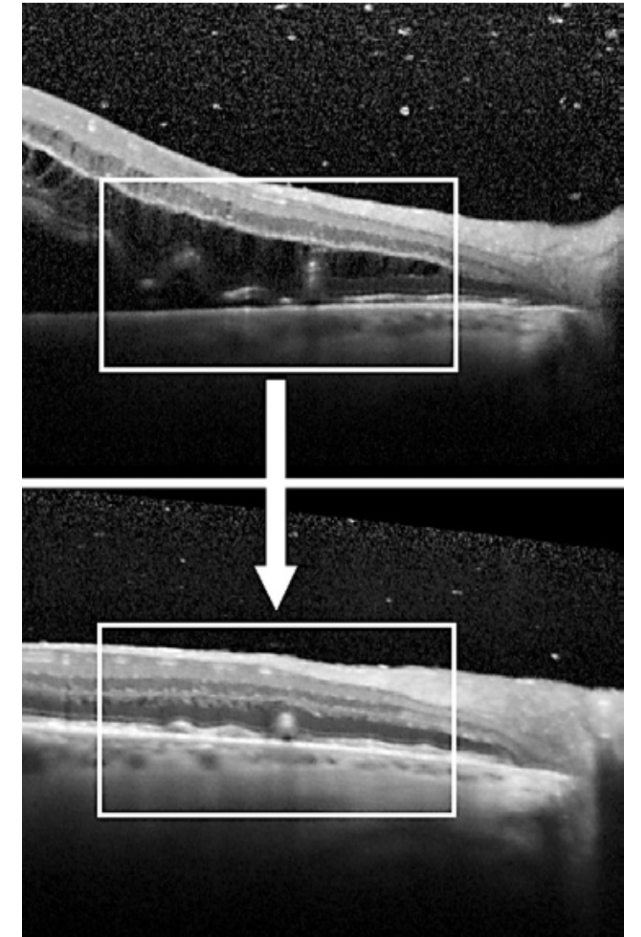
1. Yeo, Y.D., Kim, Y.C. Significance of outer retinal undulation on preoperative optical coherence tomography in rhegmatogenous retinal detachment. *Sci Rep.* 2020; 10: 15747.

## Corrugations



Dalvin LA, Spaide RF, Yannuzzi LA, et al. Hydration Folds in Rhegmatogenous Retinal Detachment. Retin Cases Brief Rep 2020;14:355–359.

## Partial-thickness folds of the outer retina



Saleh M, Gauthier AS, Delbosc B, Castelbou M. Impact of Metamorphopsia on Quality of Life after Successful Retinal Detachment Surgery. Ophthalmologica 2018;240:121–128.

# Methods Image Analysis

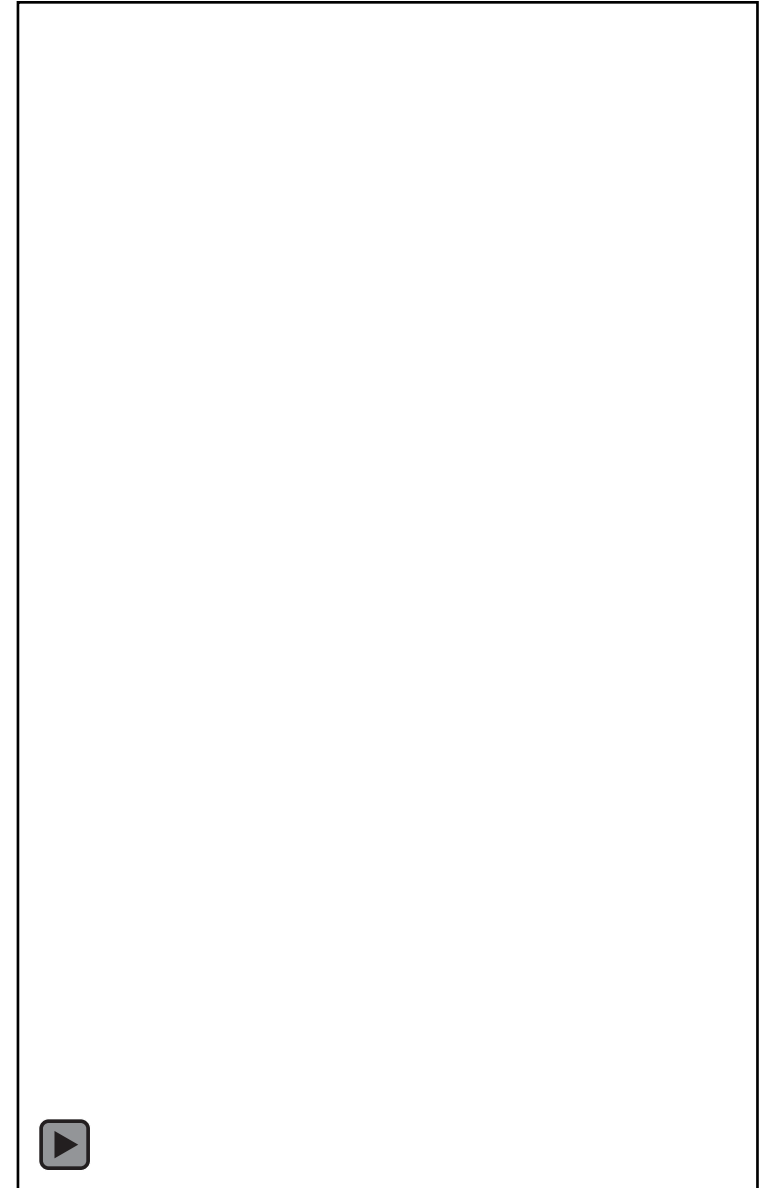
## Outer retinal folds

### En face images

- Manually segmented with slabs at a thickness of 35 to 65  $\mu\text{m}$  and positioned between the outer nuclear layer and the EZ.

### Dynamic video SD-OCT images

- Hyperreflective curvilinear or oblique lines that project above the retinal pigment epithelium has been described as the “jumping fish” sign.



# Results

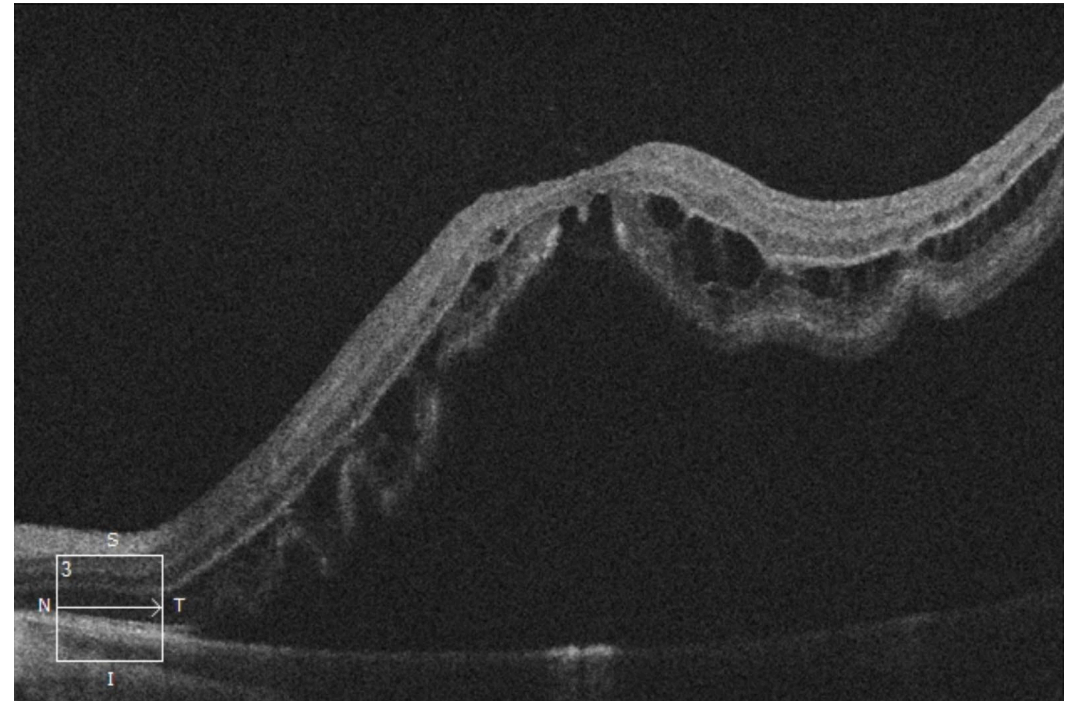
Eighty-eight eyes with **macula-off RRD** from **88 patients** included.

Variable	
Age, years, median (IQR)	62 (57-67)
Female sex, no. (%)	33 (38)
Study eye, right, no. (%)	43 (49)
Lens status, phakic, no. (%)	58 (66)
No. of quadrants of retinal detachment, mean (SD)	2.1 (0.75)
Baseline visual acuity, median, logMAR (IQR)	2 (0-2)
Primary procedure, PPV, no. (%)	44 (50)

Variable*	
Anatomical success, no. (%)	
Primary	65 (87)
Secondary	73 (97)
ETDRS, median (IQR)	
3 months	71 (58-78)
6 months	73 (61-82)
12 months	77 (71-83)
M-Charts, 12 months, median (IQR)	
MV	0.1 (0-0.35)
MH	0.2 (0-0.3)
Lens Status, pseudophakic at 12 months, no. (%)	60 (73)

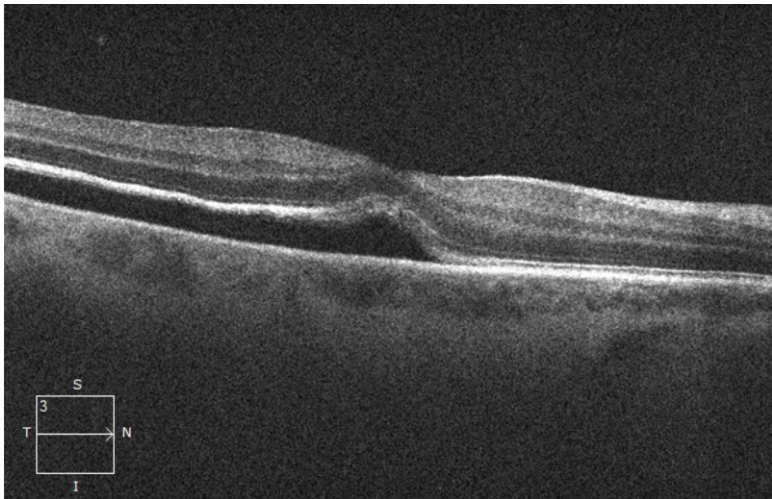
# Results

- The median duration of visual symptoms from onset to RRD repair was 95 hours (IQR: 38-478).
- Duration of visual symptoms was significantly longer in eyes with presence of outer retinal corrugations ( $p=0.001$ ).
- Eyes with retinal corrugations at baseline had higher metamorphopsia scores at 12 months ( $p=0.013$ ).

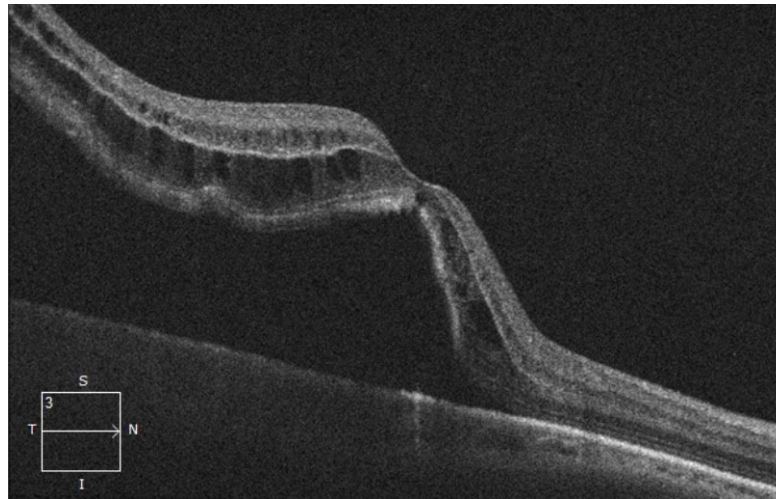


# Results

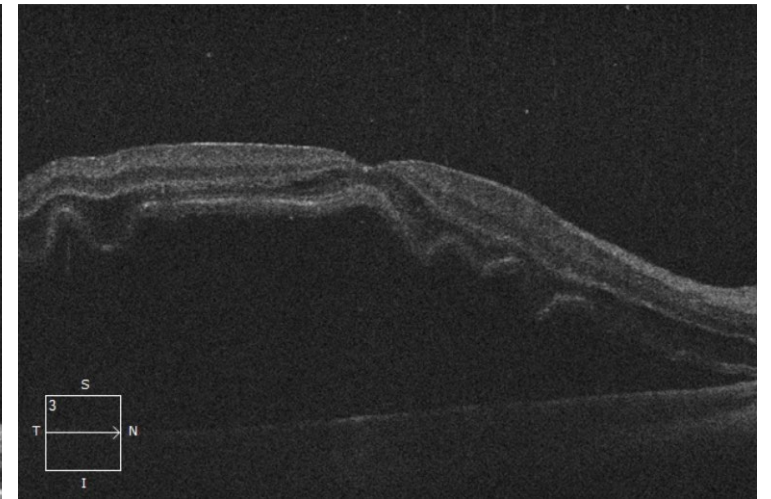
- Eyes with preoperative SRF height of  $>825 \mu\text{m}$  were more likely to have outer retinal corrugations (OR: 14,  $p < 0.001$ ).



SRF height =  $180 \mu\text{m}$



SRF height =  $746 \mu\text{m}$



SRF height =  $867 \mu\text{m}$

# Results

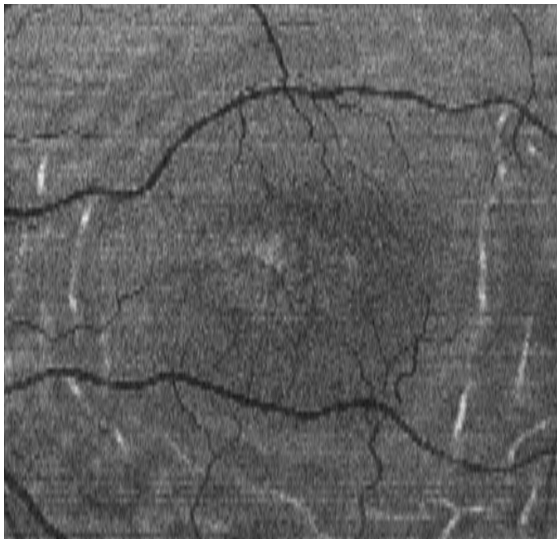
Variable	Univariate Analysis				Multivariate Analysis			
	B <sup>a</sup>	95% CI	beta	<i>p</i>	B <sup>a</sup>	95% CI	beta	<i>p</i>
<b>3 months</b>								
SRF height > 825 μm	-16.5	-27 to -6.1	-0.456	<b>0.003</b>	-15.5	-25.6 to -5.3	-0.428	<b>0.004</b>
Lens status					10.7	-0.573 to 22	0.266	0.062
<b>12 months</b>								
SRF height > 825 μm	-8.8	-17.3 to 0.253	-0.333	<b>0.044</b>	-8.5	-17.3 to 0.279	-0.324	0.057
Lens status					2.7	-7.1 to 12.4	0.091	0.585
<sup>a</sup> Unstandardized								

SRF height classified as high (>825 μm, the 50th percentile) or low (≤825 μm).

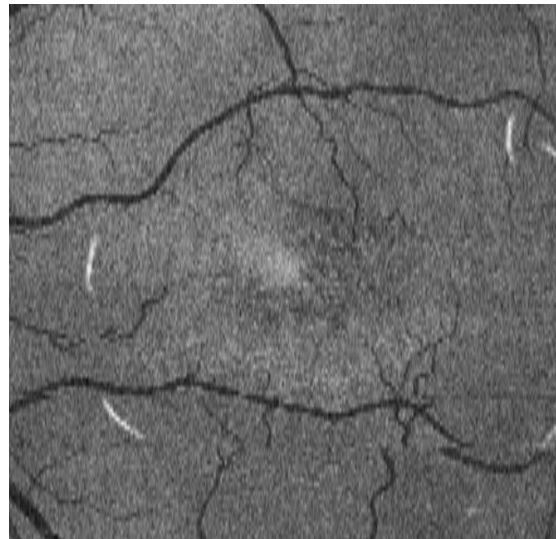
# Results

- Presence of ORFs or “jumping fish” sign was detected in 47% of eyes at 1-month follow-up.
- Detectable ORFs ↓ to 19%, 8%, and 3% at 3, 6 and 12-month follow-ups, respectively.

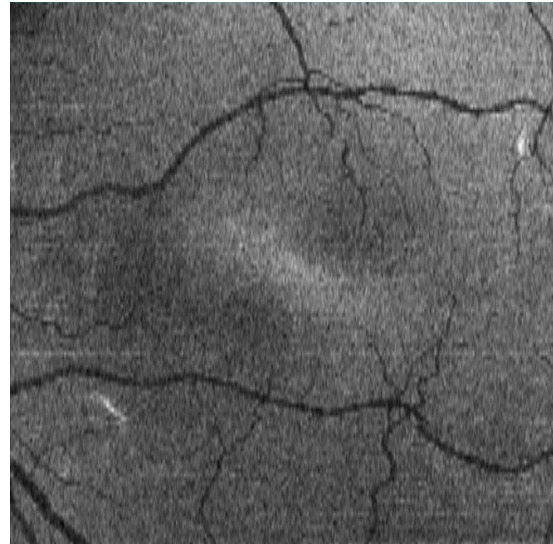
1 month



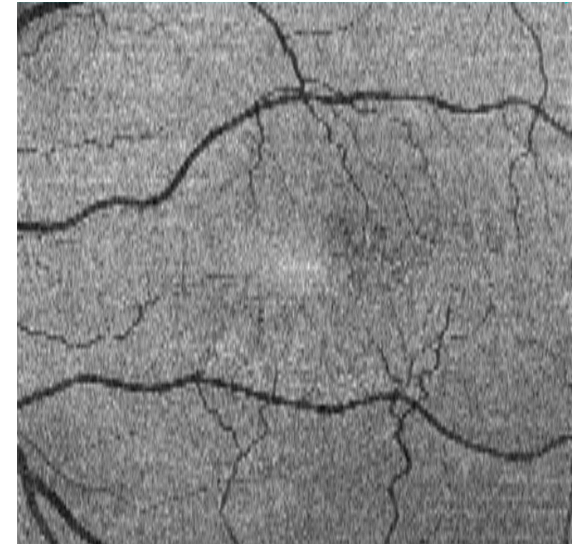
3 months



6 months



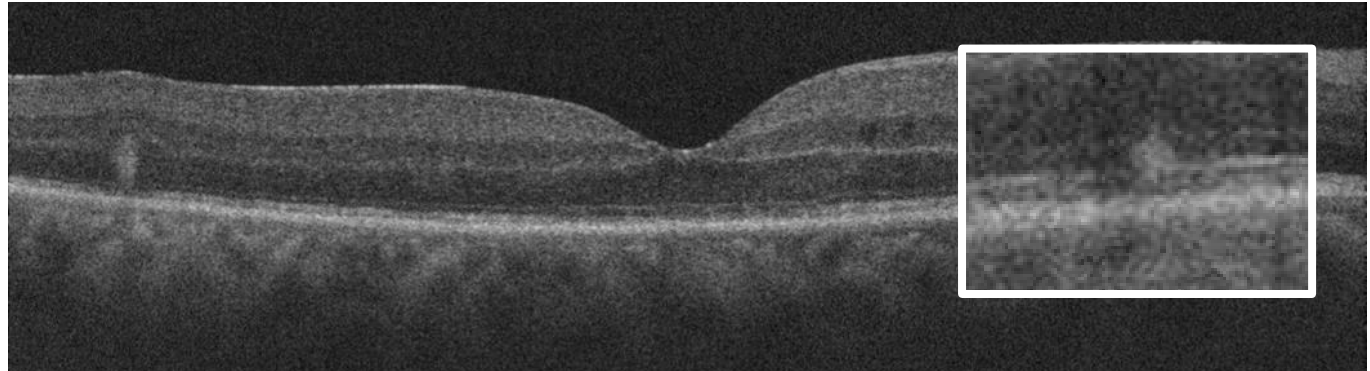
12 months





# Results

- The presence of ORFs at 6 months was associated with interruptions in outer retinal integrity on cross-sectional SD-OCT scans at 12 months.
  - ELM ( $p=0.036$ )
  - EZ ( $p=0.018$ )
  - IZ ( $p=0.016$ )

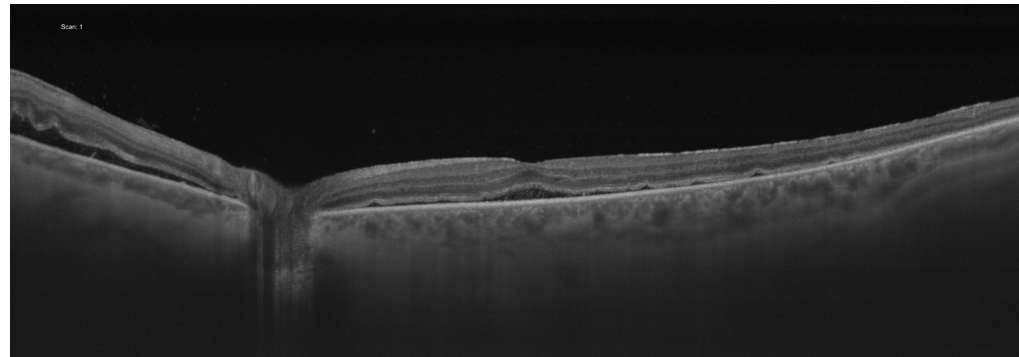
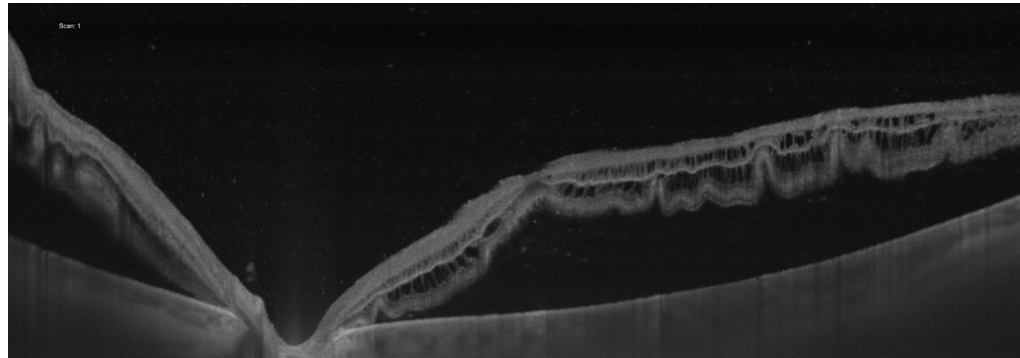
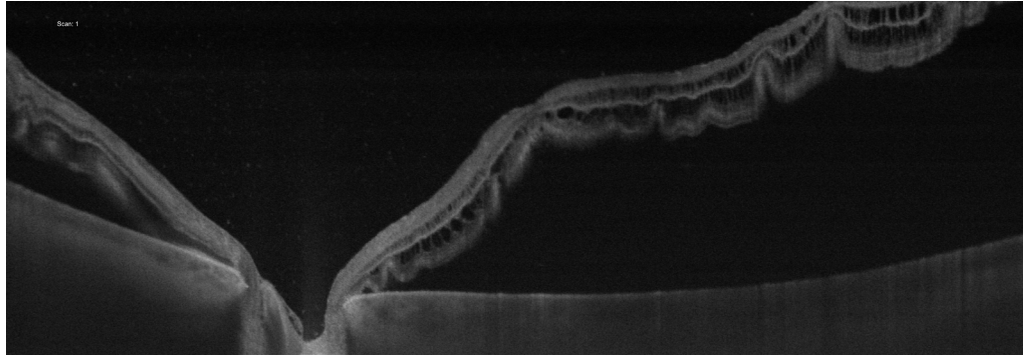


- Persistent ORFs at 6 months were suggestive of a lower ETDRS at 12 months ( $p<0.004$ ).
- Persistent ORFs also increased chance of having any metamorphopsia at 12 months ( $p=0.032$ ).



# Implications

- Timing of surgical repair
- Surgical technique
- Prediction of long-term outcomes
- Patient counselling



# Future Directions

# Conclusions

- Baseline and early post-operative outer retinal findings on en face and cross-sectional OCT may serve as useful biomarkers for long-term visual prognosis following macula-off RRD repair.

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Thank You!

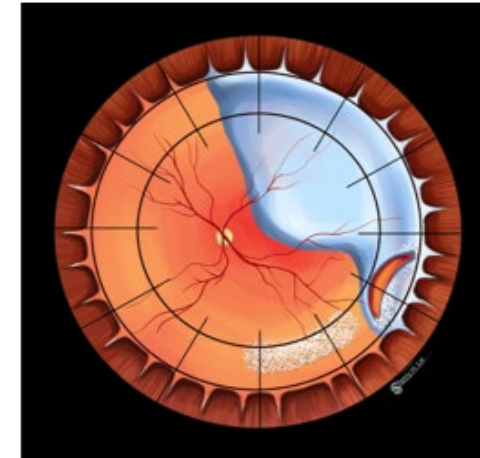
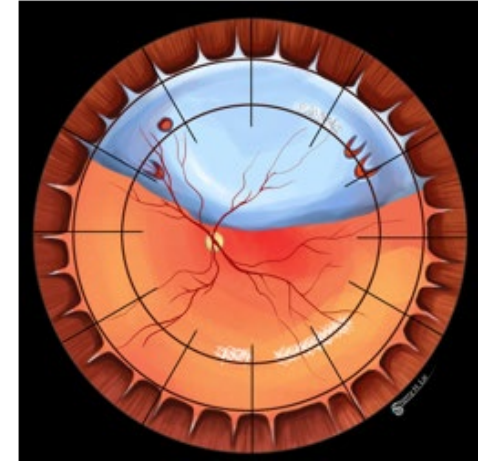
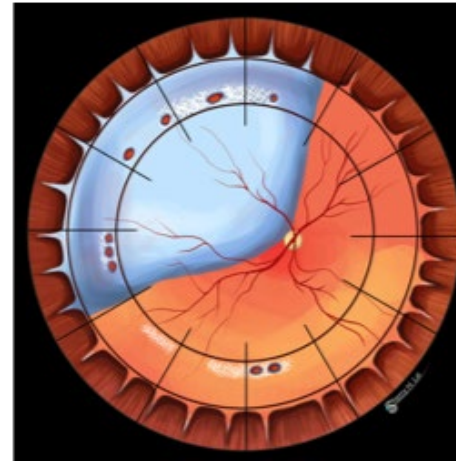
tina.felfeli@mail.utoronto.ca  
@TinaFelfeli

# Appendices

# Exclusion Criteria

## Exclusion criteria:

- Inferior breaks in detached retina
- Significant media opacity (e.g. vitreous hemorrhage or cataract preventing detailed retinal examination)
- Proliferative vitreoretinopathy (PVR) grade B or worse
- Previous retinal detachment (index eye)
- Previous PPV (index eye)
- Age <18 years
- Mental incapacity
- Inability to read English language
- Pre-existing ocular diagnosis that would impact on visual outcome
- Physical inability to posture post-operatively (note: patients who were simply hesitant about strict post procedural posturing were still encouraged to participate).

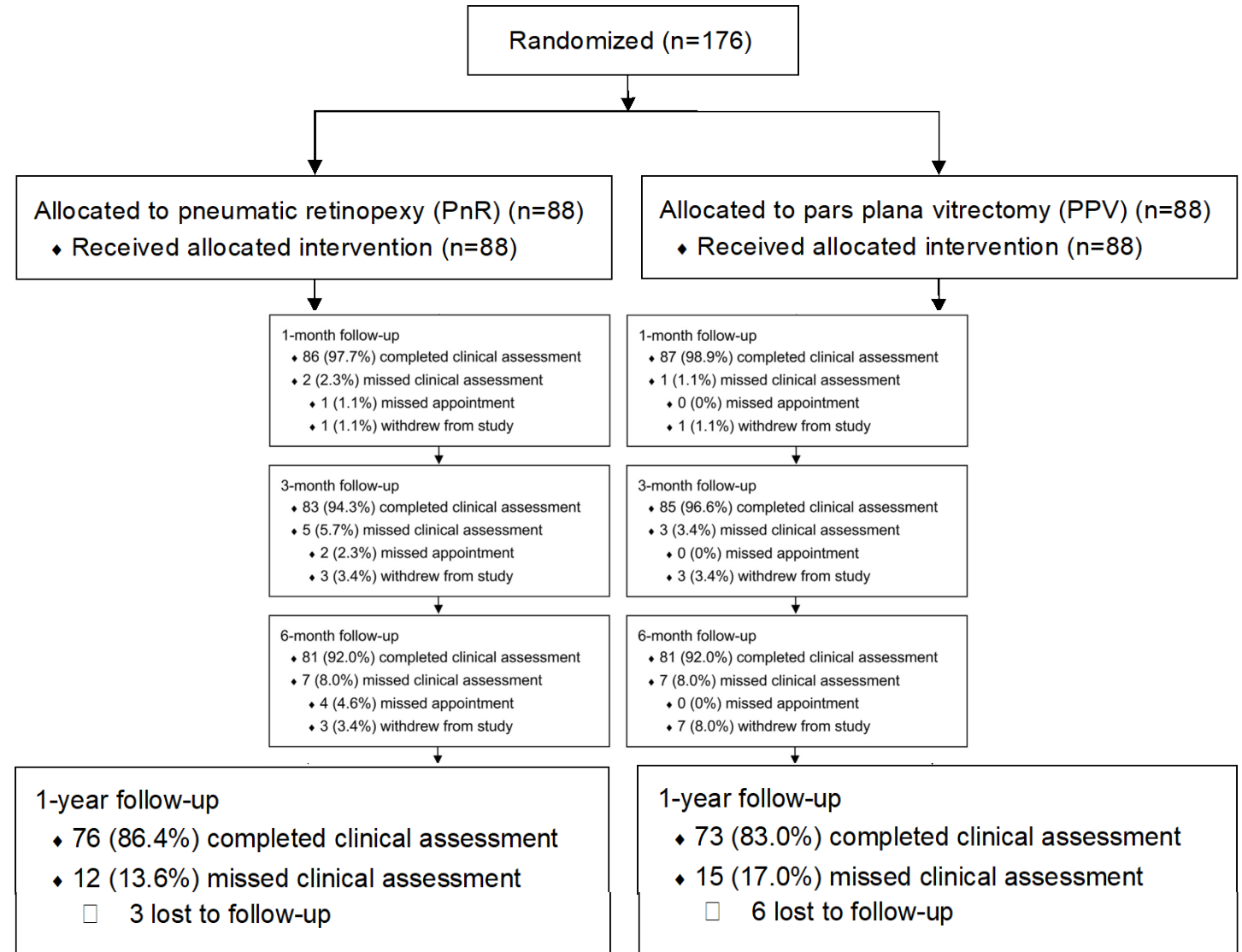




# Methods

## Study visits

- Patients were followed for up to 1 year with standard study visits at 1 month, 3 months, 6 months and 12 months.

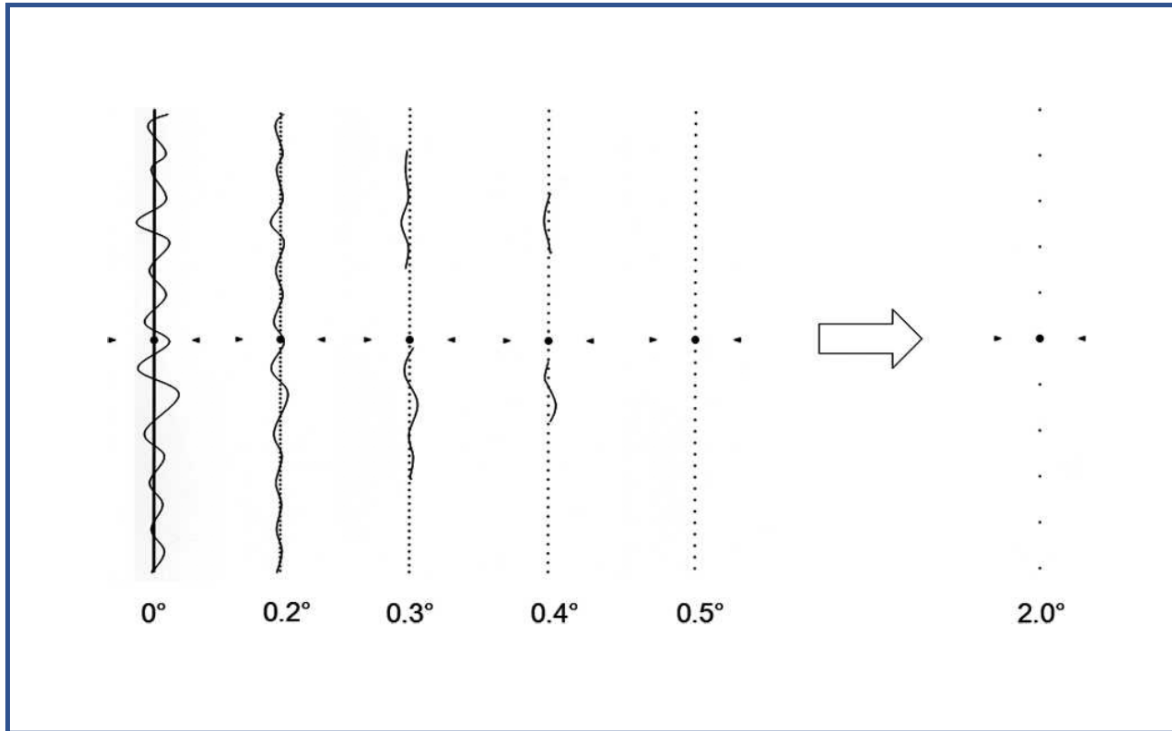


# Methods

## Statistical Analysis

- Chi-square test and t-tests for categorical and continuous data, respectively, when the data were normally distributed. Fisher's exact test was used in place of the chi-square test when expected cell counts were less than 5.
- The Mann-Whitney U test was used for continuous data that was not normally distributed.
- Pearson r correlations, univariate and multivariate regression analyses were conducted to determine associations.

# Methods Metamorphopsia



## M-CHARTS

- Vertical (MV) and horizontal (MH) metamorphopsia
- 19 dotted ( $0.1^\circ$ ) lines with dot intervals ranging from  $0.2^\circ$  to  $2.0^\circ$  of visual angle.
- Minimum angle of the dots in the line that appeared straight was taken to be the metamorphopsia score.

# Repair Techniques

- **PnR:** Most patients underwent a so-called steam-roller maneuver to expedite retinal reattachment (by pushing some sub-retinal fluid [SRF] through the retinal break) and to protect the macula from displaced SRF. The authors favor SF6 gas for PnR because it reaches maximum size rapidly and has a shorter duration until dissipation.
- **PPV:** Subretinal fluid generally was drained through the break responsible for the retinal detachment, after marking it with endodiathermy. However, the use of heavy liquid or posterior retinotomy were at the surgeon's discretion. A complete air-fluid exchange was performed, and isoexpansile SF6 or perfluoropropane gas was injected. Generally, SF6 was preferred, with perfluoropropane used in patients with inferior pathologic features or traction evident at the time of surgery. The use of adjunctive surgical techniques, such as placement of a scleral buckle, silicone oil, or combined cataract extraction, were permissible but were used rarely. Patients were placed face down immediately after PPV, except in macula-attached patients with no SRF close to the posterior pole at the end of surgery, in which case they were positioned according to the location of the retinal break.

# En Face

- The software application takes dense raster scans and reconstructs a C-scan image on the coronal plane.
- The lesions can be specified within the subretinal layers.

# Timing of Surgery

- Controlled setting in PIVOT: Time to the allocated intervention was dependent on macular status: within 24 macula detached cases.
- Earlier surgery for RRD may be associated with better functional recovery (decreased SRF height and development of corrugations).

# Reductions in final visual acuity occur even within the first 3 days after a macula-off retinal detachment

Greven MA, Leng T, Silva RA, et al. Reductions in final visual acuity occur even within the first 3 days after a macula-off retinal detachment. Br J Ophthalmol 2018:1–4.

# PnR vs PPV

- The prevalence of ORFs did not differ between PnR and PPV.
  - 1 month: PnR, 27% vs PPV, 40% (p=0.199)
  - 3 months: PnR, 24% vs PPV, 13% (p=0.217)
  - 6 months: PnR, 18% vs PPV, 5% (p=0.076)
  - 12 months: PnR, 11% vs PPV, 9% (p=0.749)



# ERM

- Presence of ERM at 3, 6, and 12 months not associated with ETDRS VA.
  - 3 months,  $p=0.301$
  - 6 months,  $p=0.252$
  - 12 month,  $p=0.925$
- Presence of ERM at 3, 6, and 12 months not associated with ORFs.
  - 3 months,  $p=0.103$
  - 6 months,  $p=0.333$
  - 12 months,  $p=0.178$

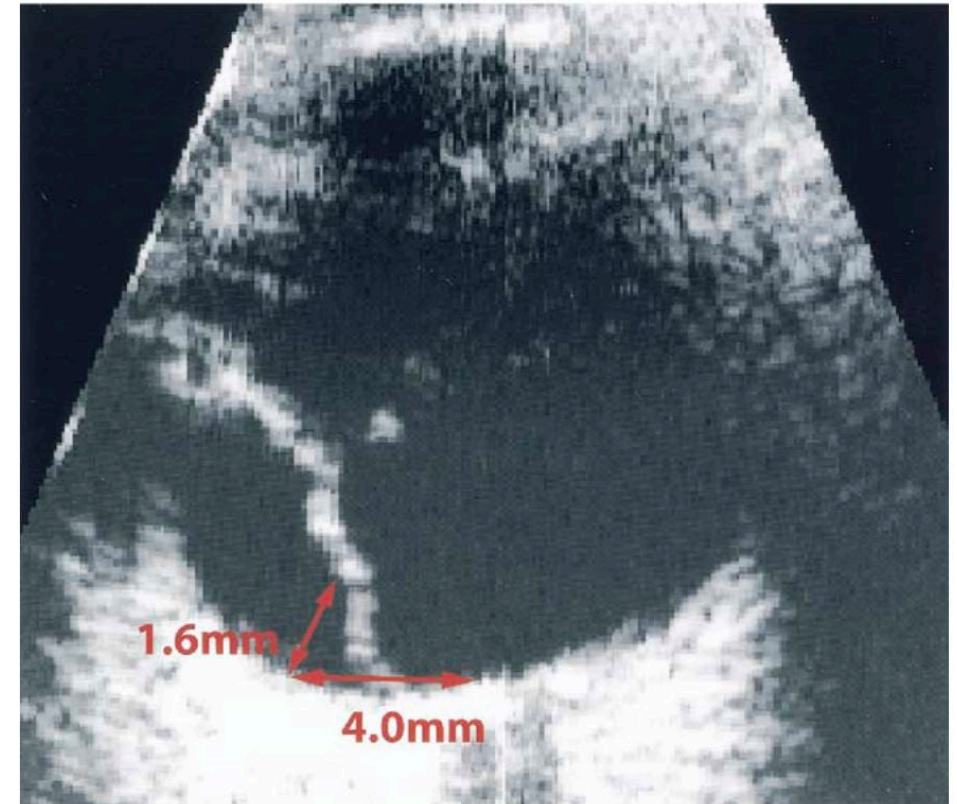
# Prevalence of Baseline Features

- SRF height  $>825 \mu\text{m}$ : 53%
- Intraretinal cystic cavities: 84%
- Corrugations: 80%

## The Correlation between Height of Macular Detachment and Visual Outcome in Macula-Off Retinal Detachments of $\leq 7$ Days' Duration

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Ross W, Lavina A, Russell M, Maberley D. The correlation between height of macular detachment and visual outcome in macula-off retinal detachments of  $\leq 7$  days' duration. *Ophthalmology* 2005;112:1213–1217.



**Figure 2.** Patient 40, with a macular height of 1.6 mm. Preoperative vision, 20/400; postoperative vision, 20/100.

# RELATIONSHIP BETWEEN PREOPERATIVE FOVEAL MICROSTRUCTURE AND VISUAL ACUITY IN MACULA-OFF RHEGMATOGENOUS RETINAL DETACHMENT

## Imaging Analysis by Swept Source Optical Coherence Tomography

HIROSHI NODA, MD, SHUHEI KIMURA, MD, PhD, YUKI MORIZANE, MD, PhD, SHINJI TOSHIMA, MD,  
MIO MORIZANE HOSOKAWA, MD, YUSUKE SHIODE, MD, PhD, SHINICHIRO DOI, MD,  
KOSUKE TAKAHASHI, MD, MIKA HOSOGI, MD, ATSUSHI FUJIWARA, CO, PhD,  
FUMIO SHIRAGA, MD, PhD

“In macula-off rhegmatogenous retinal detachment, preoperative continuity of the ELM and EZ may be a predictor of postoperative best-corrected visual acuity.”

# OUTER RETINAL FOLDS FOLLOWING PARS PLANA VITRECTOMY WITH MEMBRANE PEEL

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Nicholas A. Iafe, BA,\* Simon Law, MD,\* David Sarraf, MD,\*† Irena Tsui, MD\*

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**Purpose:** To report a case of outer retinal folds following pars plana vitrectomy with epiretinal membrane peel.

**Methods:** Retrospective case report. Spectral-domain and en face optical coherence tomography findings are described.

**Results:** A 54-year-old man presented with distorted vision 1 month following pars plana vitrectomy with epiretinal membrane peel and subsequent cataract extraction. Optical coherence tomography of the affected eye revealed ripple-type and taco-type outer retinal folds. En face optical coherence tomography illustrated a curvilinear characteristic pattern of the folds that spontaneously resolved with follow-up.

**Conclusion:** The authors report a case of outer retinal folds developing in a patient following pars plana vitrectomy with membrane peel. En face optical coherence tomography findings of outer retinal folds may enhance diagnosis.

**RETINAL CASES & BRIEF REPORTS 11:S31–S33, 2017**

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# **METAMORPHOPSIA AND OUTER RETINAL MORPHOLOGIC CHANGES AFTER SUCCESSFUL VITRECTOMY SURGERY FOR MACULA-OFF RHEGMATOGENOUS RETINAL DETACHMENT**

Okuda T, Higashide T, Sugiyama K. Metamorphopsia and Outer Retinal Morphologic Changes After Successful Vitrectomy Surgery for Macula-Off Rhegmatogenous Retinal Detachment. *Retina*. 2017;0:1-7.

Restoration of both the ellipsoid zone and interdigitation zone bands seems to be an important factor for the reduction of metamorphopsia after successful vitrectomy for macula-off RRD.

# Prevalence and predictors of metamorphopsia after successful rhegmatogenous retinal detachment surgery: a cross-sectional, comparative study

Zhou C, Lin Q, Chen F. Prevalence and predictors of metamorphopsia after successful rhegmatogenous retinal detachment surgery: a cross-sectional, comparative study. *Br J Ophthalmol.* 2017;101:725-729.

The postoperative presence of SRF and disrupted ELM line are independent predictors of metamorphopsia.

# EARLY SIMULTANEOUS FUNDUS AUTOFLUORESCENCE AND OPTICAL COHERENCE TOMOGRAPHY FEATURES AFTER PARS PLANA VITRECTOMY FOR PRIMARY RHEGMATOGENOUS RETINAL DETACHMENT

Dell’Omo R, Mura M, Lesnik Oberstein SY, et al. Early simultaneous fundus autofluorescence and optical coherence tomography features after pars plana vitrectomy for primary rhegmatogenous retinal detachment. *Retina* 2012;32:719–728.

The presence of outer retinal folds most commonly seen at 1 month, is significantly related to metamorphopsia but did not relate to poor postoperative visual acuity.